REMARKS

Claims 14-29 are pending. Claims 14, 16, 23 and 25 have been amended. Claims 1-13 were previously cancelled.

The Claims Are Not Obvious over the Prior Art of Record

Claims 1-22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Deihl (WO 94/13280) in view of Fassberg et al (EP 0656206) and further in view of Kanios et al (U.S. Patent No. 5,719,197).

The PTO relies on Deihl as teaching a sprayable analgesic composition where the analgesic is capable of being absorbed into the bloodstream through the buccal mucosa. The PTO states that Deihl teaches that the analgesic is ibuprofen or acetaminophen and the liquid carrier is aqueous ethanol. The PTO further relies on Table I as showing the concentration range of each ingredient. (Office Action at 2).

The PTO acknowledges that, beyond the disclosed analgesics and solvent, Deihl does not disclose any other suitable active agent or the use of any other solvents. Deihl does not disclose the specific solvents of Applicant's dependent claims. Deihl also does not disclose any of a central nervous system active amine, a sulfonyl urea, an antibiotic, an antifungal, an antiviral, a sleep inducer, an antiasthmatic, an antiemetic, a histamine H-2 receptor antagonist, a barbiturate, a prostaglandin or a bronchial dilator as claimed in the present application. In order to overcome these deficiencies, the PTO relies on Fassberg and Kanios.

According to the PTO,

> It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general

> teachings of formulations for buccal mucosal administration, to have looked in the art for other specific solvents suitable for spray formulations of liquid carriers, as taught by Fassberg et al, with reasonable expectations of successfully preparing suitable formulations for various therapies. Furthermore it is obvious to one of ordinary skill in the art to have substituted any suitable active agent for the analgesics of Diehl's buccal spray formulations as claimed as taught by Kanios et al.

Office Action at 3. For at least the following reasons, this rejection should be withdrawn.

As acknowledged by the PTO, Deihl does not disclose solvents other than ethanol or other suitable active agents beyond ibuprofen and acetaminophen. Deihl does not disclose or suggest the inclusion of a central nervous system active amine, a sulfonyl urea, an antibiotic, an antifungal, an antiviral, a sleep inducer, an antiasthmatic, an antiemetic, a histamine H-2 receptor antagonist, a barbiturate, a prostaglandin or a bronchial dilator. There is simply no teaching or suggestion in Deihl to include any active agent other than ibuprofen or acetaminophen.

Furthermore, Applicant's independent claims recite compositions and methods for spraying the oral mucosa of the mammal with a propellant free buccal spray composition, containing a pharmacologically active compound and "between 30 and 99.69 percent" of a pharmacologically acceptable solvent. The PTO states that "[t]he table in example I [of Deihl] shows the concentration ranges of each ingredient." Office Action at 2. Example I of Deihl, however, discloses that the composition includes only 8.08% solvent (50 parts SD alcohol per 618.82 total parts).

In contrast to Deihl, the present independent claims recite propellant free buccal spray compositions and methods requiring a pharmacologically active

compound and "between 30 and 99.69 percent" of a polar solvent. There is nothing in Deihl that discloses or suggests including more than the 8.08% solvent disclosed in Example I of Deihl.

Fassberg relates to an inhalation aerosol, which is a propellant-containing spray or powder formulation for oral and/or nasal administration, including actives such as antihistamines, antiallergics, analgesics, antibiotics, steroids, and bronchodilators for treating asthma. Fassberg does not disclose or suggest any propellant-free composition or any method for the delivery of an active agent by spraying the oral mucosa of a mammal with a propellant free buccal spray composition, to provide transmucosal absorption of a pharmacologically effective amount of any active compound to the systemic circulatory system through the oral mucosa.

According to the PTO, it would have been obvious "to have looked in the art for other specific solvents suitable for spray formulations of liquid carriers, as taught by Fassberg, with reasonable expectations of successfully preparing suitable formulations for various therapies." (Office Action at 3.) The PTO overlooks that the Applicant's claims are to propellant-free compositions and methods of buccal administration. In contrast, Fassberg's compositions are inhalants, which are necessarily formulated and administered differently than the claimed buccal spray compositions and methods. For one thing, Fassberg requires a propellant, which is expressly excluded from all pending claims of the present application. Furthermore, one of ordinary skill would not have looked to Fassberg for solvents to apply in the formulations of Diehl, because Fassberg explains that the solvents used in its inhalation formulations are only present to facilitate the propellant. As the Office Action acknowledges, Diehl has no propellant. In addition, there is no disclosure or suggestion in the cited references that any formulations of active agents other than Diehl's acetaminophen and ibuprofen could be

administered in pharmacologically effective amounts to the systemic circulatory system via absorption through the oral mucosa. There is no suggestion or motivation in Fassberg to apply its active agents or solvents in the method or formulation of Deihl. To the contrary, Fassberg formulates its actives for administration, and administers its actives, via inhalation (using a propellant).

Kanios does not cure the deficiencies of Diehl and Fassberg. Kanios merely refers to a dosage form having a flexible backing that can be prepared using a spray as an intermediate. Kanios says nothing about any buccal spray dosage form or related method.

The PTO states that Kanios "teaches formulations that can be in a spray format." In contrast to the present invention, the finished dosage form of Kanios is made of an active agent and either a finite or non-finite pharmaceutical carrier (i.e., the "resulting mixture" in col. 9, lines 21 and 23). There is no disclosure in Kanios that the "resulting mixture" is administered directly to the oral mucosa in any form, much less as a spray. According to Kanios, the composition is made into a "finished dosage form" by applying a flexible backing which further defines the size and shape of the finished dosage form, which is, among other things, occlusive to water permeation in vivo. In contrast to the present invention, Kanios never discloses that its finished dosage form is a spray, much less a spray composition or method capable of providing a systemic effect.

At column 10, lines 57-65, Kanios refers to appropriate "sizes" of the composition and the amount of agent per "surface area" of the finished dosage form. That this paragraph of Kanios also refers to mg/ml concentrations for anesthetic agents is in no way a disclosure of a spray final dosage form. The intermediate resulting mixture of Kanios will have a concentration of active when added to an adhesive,

backed by a flexible backing, or otherwise made into the finite finished dosage form of Kanios. Therefore, simply because an anesthetic agent concentration is disclosed, does not disclose or suggest a finished dosage form suitable for spraying on the oral mucosa. Such a spray dosage form is never contemplated or taught by Kanios.

While Kanios refers to a list of pharmaceutical agents, there is, however, no disclosure or suggestion of a spray dosage form composition or methods capable of providing transmucosal absorption of an active compound to the systemic circulatory system through the oral mucosa, as presently claimed.

The PTO has not provided any motivation, beyond the impermissible hindsight use of Applicant's specification as a roadmap, to pick and choose from the relied upon references to arrive at the claimed invention. Courts have generally recognized that a showing of a *prima facie* case of obviousness necessitates three requirements: (i) some suggestion or motivation, either in the references themselves or in the knowledge of a person of ordinary skill in the art, to modify the reference or combine the reference teachings; (ii) a reasonable expectation of success; and (iii) the prior art references must teach or suggest all claim limitations. See e.g., In re Dembiczak, 175 F.3d 994 (Fed. Cir. 1999); In re Rouffet, 149 F.3d 1350, 1355 (Fed. Cir. 1998); Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573 (Fed. Cir. 1996). Applicants further note that in order to establish a *prima facie* case of obviousness, "[i]t is insufficient that the prior art disclosed the components of the patented device, either separately or used in other combinations; there must be some teaching, suggestion, or incentive to make the combination made by the inventor." Northern Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 934 (Fed. Cir. 1990). This way, "the inquiry is not whether each element existed in the prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed." Hartness Int'l, Inc. v. Simplimatic Engineering Co.,

819 F.2d 1100, 1108 (Fed. Cir. 1987). Accordingly, a determination of obviousness "must involve more than indiscriminately combining prior art; a motivation or suggestion to combine must exist." Pro-Mold & Tool Co., 75 F.3d at 1573. Here, the PTO has not met its burden of showing a *prima facie* case of obviousness against the pending claims. There is no motivation to combine the buccal spray of Deihl with the nasal/inhalation spray of Fassberg and the adhesive-backed dosage form of Kanios to arrive at the claimed propellant-free buccal spray compositions or the claimed methods of delivering specific actives in pharmacologically effective amounts to the systemic circulatory system through the oral mucosa.

All of Applicant's pending claims require "propellant-free" buccal spray compositions and related methods. There is no teaching or suggestion in the cited references that would have motivated the skilled artisan to remove the propellant from the Fassberg inhalation formulations. And, even if there were such teaching, there would be no reason to retain any polar excipients as these are only present in Fassberg to "facilitate[] the compatibility of the medicament with the propellant and also lower[] the discharge pressure to an acceptable range." Fassberg at page 4, lines 52-53. Thus, if the propellant is removed from the Fassberg formulations -- and it cannot be -- then the polar excipient should also be removed, as there is no disclosure or suggestion in Fassberg to retain these excipients for any reason other than to facilitate compatibility with the propellant. Consequently, even if Fassberg is combined with Diehl, one of ordinary skill would still not have any propellant-free compositions or methods utilizing the polar solvents and ranges claimed by Applicant.

In addition, as the Office Action acknowledges, Fassberg is solely directed to inhalation formulations. The formulations are fashioned in such a way as to ensure that the active ingredient will "reach the lungs." Fassberg at page 5, lines 50-55. As the

Office Action acknowledges, the Fassberg formulations contain "pharmaceutically active compounds which are to be delivered by oral inhalation or nasally." (Fassberg at page 5, lines 42-43, emphasis added.) In contrast, the present claims recite buccal spray compositions and methods, wherein a "pharmacologically effective amount" of the active is provided "to the systemic circulatory system via absorption through the oral mucosa." The inhalation formulations of Fassberg are not intended to and cannot provide a pharmacologically effective amount of any active systemically via absorption through the oral mucosa, as required by the pending method claims.

Consequently, no proper combination of Fassberg, Diehl, and Kanios would have provided all of the required limitations of Applicant's independent composition or method claims. Furthermore, there is no motivation for one of ordinary skill in the art to combine the solvents of Fassberg's propellant-containing inhalation formulations and the actives of Kanios' adhesive-backed dosage forms with the compositions of Diehl, and any such combination would be improper as Fassberg's solvents and ranges are only present to facilitate a propellant (which is excluded from all of the presently claimed formulations and methods) so that the actives of Fassberg can reach the lungs. The person having ordinary skill in the art would have found no motivation to combine the disclosures of the cited references, other than the use of Applicant's specification as a roadmap, to arrive at the claimed invention. In order for an obviousness rejection to be proper, there must be some suggestion or motivation, either in the references themselves or in the knowledge of a person of ordinary skill in the art, to modify the reference or combine the reference teachings. Here, there is none.

The Examiner states that "one cannot show nonobviousness by attacking references individually where the rejections are based on a combination of references." Office Action at 5. However, Applicant has not merely distinguished each reference

individually. While there are significant differences between each reference and the pending claims, Applicant also has explained and established for the record that no proper combination of the cited references can achieve what Applicant has achieved. Any rejection under U.S.C. § 103 using the cited references is based on the improper hindsight use of Applicant's own disclosure.

For the above reasons, Applicant respectfully requests that the rejections under 35 U.S.C. § 103(a) of the independent claims be reconsidered and withdrawn. Each of Applicant's dependent claims is allowable for at least the same reasons.

Obviousness-type Double Patenting Rejection

Claims 1-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 27-34, 54-49 and 80-82 of co-pending application no. 09/537,118 in view of Kanios et al. (U.S. Patent No. 5,719,197). Applicant notes that application no. 09/537,118 is still pending and is not currently allowed. As this is only a provisional rejection and no other rejections are currently outstanding, Applicant respectfully requests that the provisional rejection be withdrawn.

Examiner's Note

The Examiner also notes that certain concentration ranges recited in various dependent claims do not correspond to concentration ranges stated in the specification. Applicant points out that all originally claimed concentration ranges are well supported by the specification. The Examiner has not "noted" that the broadest claimed ranges do not correspond to ranges stated in the application. In fact, the Examiner only takes issue with narrower ranges, which fall within Applicant's broadly supported ranges.

The amendments requested by the Examiner amount only to stating particular ranges with greater precision.

It is Applicant's position that no amendments of the recited concentration ranges are necessary for allowance of any claims. While the Examiner's note is not a proper rejection or objection, in order to further prosecution of this application, Applicant has amended claims 14, 16, 23 and 25. By these amendments, Applicant does not disclaim any subject matter. In fact, the scope of the claims has been broadened.

Conclusion

In view of the above, Applicant believes the pending application is in condition for allowance. If the Examiner should believe that anything further may be required to place this application in even better form for allowance, she is cordially invited to telephone the Applicant's undersigned representative.

Dated: June 29, 2006

Respectfully submitted,

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